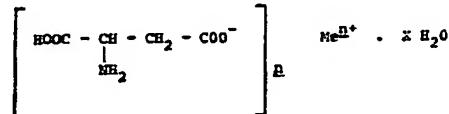

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John H. Perry's *Chemical Engineers' Handbook*,
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(54) Recovering salts of aspartic acid

(57) The invention relates to a process for recovering salts of aspartic acid corresponding to the general formula



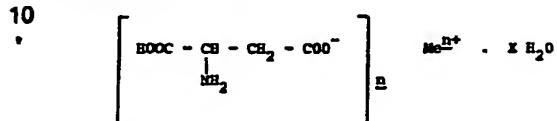
In which either $n = 1$ and Me is an alkali metal or $n = 2$ and Me is an alkaline earth metal or a divalent heavy metal and X represents an integer or a fractional number having a value of from 0 to 4, depending on the cation present, which comprises spray drying a solution of the salt at temperatures in the range from 500°C to 20°C. Preferably the spray drying is carried out at temperatures in the range from 300°C to 80°C.

The salts are obtained in a substantially quantitative yield and in highly pure form during spray drying.

SPECIFICATION**Process for recovering salts of aspartic acid**

5 This invention relates to a process for recovering salts of aspartic acid.

More particularly the invention relates to a process for recovering salts of aspartic acid corresponding to the general formula



15 in which either $n = 1$ and Me is an alkali metal or $n = 2$ and Me is an alkaline earth metal or a divalent heavy metal and X represents an integer or fractional number having a value of from 0 to 4, depending on the cation present.

The alkali metal, alkaline-earth metal and heavy-metal salts of aspartic acid are of considerable importance as active principles of medicaments and as constituents of infusion solutions. They are readily soluble in water and organic solvents or in mixtures of water and organic solvents in which salt formation is carried out. As a result, their isolation in crystalline form on a commercial scale is extremely difficult and, above all, involves heavy losses.

The process according to the invention comprises spray drying a solution of the salt at a temperature in the range from 500°C to 20°C.

The required salts are obtained both in a substantially quantitative yield and in highly pure form during spray drying. They may be directly used for any desired applications without further purification. By varying the conditions prevailing during spray drying, the salts may readily be obtained in various particle sizes with a relatively narrow particle size spectrum and with definite physical properties.

The salts recovered by the process according to the invention accumulate with the same composition as the corresponding salts isolated by the conventional crystallisation process. What is surprising above all is that, even where spray drying is carried out at temperatures over a wide range, the water of crystallisation is not removed, i.e. the salts containing water of crystallisation are obtained in the form of defined hydrates.

The process according to the invention is particularly suitable for the production of salts of aspartic acid with alkali metals, particularly lithium, sodium or potassium, with alkaline earth metals, particularly magnesium or calcium, and with divalent heavy metals, particularly zinc, iron, manganese, cobalt or copper.

Spray drying may be carried out both on solutions which have been specifically prepared for spray drying and also on the mother liquors which accumulate after the partial crystallisation of salts of aspartic acid.

The salt solutions are best prepared by reacting stoichiometric quantities of aspartic acid with the corresponding oxides or hydroxides of the metals in

water and/or organic solvents. Preferred organic solvents are alcohols containing from 1 to 8 carbon atoms, particularly methanol, ethanol or isopropyl alcohol.

70 The minimum quantity of solvent required for salt formation is dependent upon the solubility of the particular salt in the selected solvent at boiling temperature. In principle, it is possible to use salt solutions of any dilution for spray drying. For

75 economic reasons, however, it is of course best to use solutions having the highest possible concentration.

The aspartic acid may be used both in the form of its optical isomers and also in the form of the racemate.

80 Spray drying of the salt solutions may be carried out in any spray dryers of standard construction. The temperature on entry of the drying air should best not exceed 500°C, whilst the starting temperature and the product temperature should best not fall below 20°C. Drying is preferably carried out at temperatures in the range from about 300°C to 80°C.

The invention is illustrated by the following Examples.

EXAMPLE 1**Sodium-L-aspartate . H₂O**

133.1 g (1 mole) of L-aspartic acid are suspended in 200 ml of water, followed by the addition in portions of 40 g (1 mole) of NaOH. Following the addition of 10 g of active carbon, the mixture is heated for 15 minutes to reflux temperature and subsequently filtered while still hot. The colourless solution is sprayed into a spray tower at a temperature of 280°C. The solid product is removed from the spray

100 tower at a temperature of 120°C. The colourless powder is obtained in a yield of 98% (169.5g). The specific rotation $[\alpha]^{20}_{D}$ amounts to + 19.8° (10% solution in 2.5 N hydrochloric acid).

EXAMPLE 2**Magnesium-bis-L-aspartate . 2H₂O**

The salt solution is produced from 266.2 g (2 moles) of L-aspartic acid and 40.3 g (1 mole) of magnesium oxide in 300 ml of water. Spray drying is carried out at temperatures of from 300°C (on entry)

110 to 110°C (on exit). The product is obtained in the form of a colourless crystalline powder in a yield of 99.5% (322.5 g). The specific rotation $[\alpha]^{20}_{D}$ amounts to + 19.6° (2% solution in 5 N hydrochloric acid).

EXAMPLE 3**Potassium-L-aspartate . 0.5 H₂O**

A salt solution is produced from 133.1 g (1 mole) of L-aspartic acid and 56.1 g (1 mole) of KOH in ml of water. This solution is spray-dried at temperatures of from 180°C to 95°C. 175 g (99.7 % of the theoretical) of a colourless powder-form product are obtained. The specific rotation $[\alpha]^{20}_{D}$ amounts to + 18.6° (2% solution in 5 N hydrochloric acid).

EXAMPLE 4**Zinc-bis-L-aspartate . H₂O**

125 A salt solution is produced from 133.1 g (1 mole) of L-aspartic acid and 56.1 g (1 mole) of KOH in 200 ml of water. This solution is spray-dried at temperatures of from 180°C to 95°C. 175 g (99.7 % of the theoretical) of a colourless powder-form product are obtained.

130 The specific rotation $[\alpha]^{20}_{D}$ amounts to + 18.6° (2%

solution in 5 N hydrochloric acid).

EXAMPLE 5

Lithium-L-aspartate . H₂O

133.1 g (1 mole) of L-aspartic acid and 34.0 g (1 mole) of lithium hydroxide are reacted in 600 ml of water. The solution is spray dried at temperatures of from 190°C to 120°C. 154 g (98% of the theoretical) of a colourless powder are obtained. The specific rotation [α]_D²⁰ amounts to + 21° (2% solution in 5 N hydrochloric acid).

EXAMPLE 6

Calcium-bis-L-aspartate

133.1 g (1 mole) of L-aspartic acid and 37 g (0.5 mole) of calcium hydroxide are reacted in 300 ml of water. Spray drying is carried out at temperatures of from 250°C to 130°C. 301 g (89% of the theoretical) of a colourless powder are obtained. The specific rotation [α]_D²⁰ amounts to + 20.6° (2% solution in 5 N hydrochloric acid).

EXAMPLE 7

Potassium-D, L-aspartate . 0.5 H₂O

133.1 g (1 mole) of D, L-aspartic acid and 56.1 g (1 mole) of KOH are reacted in 200 ml of water. The solution is spray dried at temperatures of from 180°C to 115°C. 178 g (99% of the theoretical) of a colourless product are obtained. Its nitrogen content amounts to 7.73%, corresponding to 99.5% of the theoretical.

EXAMPLE 8

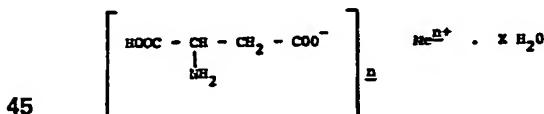
30 Magnesium-bis-D, L-aspartate . 4 H₂O

266.2 g (2 moles) of D, L-aspartic acid and 40.3 g (1 mole) of magnesium oxide are reacted in 500 ml of water. Spray drying is carried out at temperatures of from 200°C to 95°C. 352 g (98% of the theoretical) of a colourless product are obtained. The nitrogen content amounts to 7.72%, corresponding to 99.5% of the theoretical.

CLAIMS

1. A process for recovering salts of aspartic acid

40 corresponding to the general formula



in which either n = 1 and Me is an alkali metal or n = 2 and Me is an alkaline earth metal or a divalent heavy metal and X represents an integer or a fractional number having a value of from 0 to 4, depending on the cation present, which comprises spray drying a solution of the salt at temperatures in the range from 500°C to 20°C.

2. A process as claimed in Claim 1, wherein the

55 spray drying is carried out at temperatures in the range from 300°C to 80°C.

3. A process for recovering a salt of aspartic acid substantially as described with particular reference to any of the Examples.

60 4. A spray dried salt of aspartic acid when produced by a process as claimed in any of Claims 1 to 3.